REMARKS

Reconsideration and withdrawal of the rejections of the pending claims are respectfully requested in view of the amendments, remarks and enclosures herewith.

I. STATUS OF THE CLAIMS AND FORMAL MATTERS

Claims 96-116 and 127-131 are pending in this application. Claims 96-98, 100, 111-116, and 127-131 have been amended for clarity without prejudice, without admission, without surrender of subject matter and without any intention of creating any estoppel as to equivalents.

Claims 98-100 have been amended to include a space between "," and "produced" at line two. Claims 111-116 have been amended to include a "," before the word "wherein". Claims 96, and 127-131 have been amended to recite "(ii) an *in vitro* activity of at least..." Support may be found, for example, in paragraph 4 on page 3 of the Declaration from Manon Cox filed on March 24, 2004 ("the Cox Declaration") and in column 15 line 5 to column 17 line 6 of US Patent No. 6,103, 526, incorporated by reference.

No new matter is added.

The Examiner is thanked for withdrawing the previous objections to Claims 96-116 and 127-129 in the Office Action mailed May 2, 2007.

It is respectfully submitted that the claims, herewith and as originally presented, are patentably distinct over the art, and that those claims are and were in full compliance with the requirements of 35 U.S.C. § 112. The remarks made herein are not made for the purpose of patentability within the meaning of 35 U.S.C. §§101, 102, 103 or 112. Rather, the amendments and remarks herewith are made simply for clarification and to round out the scope of protection to which Applicant is entitled.

II. THE CLAIM OBJECTIONS ARE OVERCOME

Claims 98-100 and 111-116 were objected to for missing punctuation. These informalities were corrected. Claims 98-100 and 127-131 were objected to for lack of clarity, in particular, for not specifying if protein activity is in vivo or in vivo in part (ii) of the claims. These claims have been amended to clarify that the protein activity recited in part (ii) of the claims is *in vitro* activity.

Consequently, the objections to the claims are obviated.

IV. THE ART REJECTIONS ARE OVERCOME

Claims 96-97, 99-116 and claim 130 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Quelle *et al.* with evidence provided by Dorland's Illustrated Medical Dictionary, and claims 96-97, 99-116 and claim 130 were rejected under 35 U.S.C. §103(a) as allegedly obvious over Quelle *et al.* with evidence provided by Dorland's Illustrated Medical Dictionary. The rejections are respectfully traversed and will be addressed collectively.

Initially, Applicants respectfully submit that a two-prong inquiry must be satisfied in order for a Section 102 rejection to stand. First, the prior art reference must contain all of the elements of the claimed invention. *See Lewmar Marine Inc. v. Barient Inc.,* 3 U .S.P.Q.2d 1766 (Fed. Cir. 1987). Second, the prior art must contain an enabling disclosure. *See Chester v. Miller,* 15 U.S.P.Q.2d 1333, 1336 (Fed. Cir. 1990). A reference contains an enabling disclosure if a person of ordinary skill in the art could have combined the description of the invention in the prior art reference with his own knowledge of the art to have placed himself in possession of the invention. *See In re Donohue*, 226, U.S.P.Q. 619, 621 (Fed. Cir. 1985).

The Examiner contends that the said erythropoietin of Quelle *et al.* has *in vivo* activity, indicating that "silence may not be probative".

In response, Applicants respectfully submit that while the Examiner may believe that "silence may not be probative", the Examiner, who Applicants trust is familiar with the scientific process, would surely agree that probative evidence would, in this instance, constitute evidence provided by experimentation. Quelle *et al.* provides elegant *in vitro* cell culture assays along with purification, electrophoretic and protein assays, collectively used to determine the *in vitro* activity of recombinant erythropoietin (pg. 652, column 2 and pg. 653, column 1). Quelle *et al.* does not teach protein activity *in vivo.* Nowhere in the 'Material and Methods', "Results', or 'Discussion' sections of the article is there an experiment to determine or a discussion of *in vivo* erythropoietin protein activity.

While it may seem logical that the *in vitro* activity of a recombinant protein translates to *in vivo* activity, in fact, this is not typically the case. The activity of a protein *in vitro* may differ greatly from its activity *in vivo*, that is, if one is able to show that the protein exhibits *in vivo* activity at all. As recited in the following paragraph and disclosed on page 130, paragraph 2 of the Saghatelian *et al.* reference, enclosed in the Information Disclosure Statement filed

concurrently herewith, the characterization of proteins *in vitro* has several shortcomings, and to fully assess the function of a protein, proteins must be characterized in "complex biological settings":

> "The biochemical properties of proteins are typically determined in vitro with purified material. Although this classical 'test tube biochemistry' approach has succeeded in explaining the activities of many proteins, it does suffer some shortcomings. First, proteins do not function in isolation in vivo, but rather as parts of complex metabolic and signaling networks. Proteins are also regulated by post-translational mechanisms in vivo, including covalent modification and protein-protein interactions (Fig. 1). These dynamic events create a context dependency to the performance of proteins in living systems that can be difficult, if not impossible, to replicate in vitro."

In view of the foregoing, Applicants trust that the Examiner can appreciate that the demonstration of protein activity *in vitro* does **not** necessarily translate to activity *in vivo*.

Furthermore, as stated on page 8, section 6 of the Cox Declaration, the invention 'is not anticipated because ... the EPO of the present invention results in increased reticulocyte counts, indicating *in vivo* activity and stimulation of erythropoiesis regardless of the lack of sialic acid which Quelle concludes is necessary for *in vivo* activity.'

While the Examiner contends that "silence may not be probative', Applicants respectfully submit that silence regarding the existence of *in vivo* activity of the erythropoietin of Quelle *et al.* does establish that Quelle *et al.* cannot be used as an anticipatory reference under 35 U.S.C. § 102(b), as Quelle *et al.* does **not** contain **all** of the elements of the presently claimed invention, namely Quelle *et al.* does **not** teach *in vivo* protein activity.

Applicants also respectfully submit that the alleged admission 'on record that Quelle et al.'s purified recombinant erythropoietin has little, if any in vivo activity' was clearly intended to be used for the purpose of highlighting that Quelle *et al.* does **not** provide *in vivo* evidence for protein activity, and such a statement does not negate that fact that no such *in vivo* evidence is taught by Quelle *et al.*

Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. §§ 102(b) are respectfully requested.

Now turning to the rejection under 35 U.S.C. §103(a), the Examiner contends that 'the product disclosed in Quelle *et al.* would intrinsically stimulate erythropoietic activity even with 'little *in vivo* activity'. Applicants respectfully disagree and direct the Examiner to the case law,

namely that The Supreme Court has recently reaffirmed the factors set out in *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17-18: "[T]he scope and content of the prior art are determined; differences between the prior art and the claims at issue are…ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented." *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727. Furthermore, as stated by the Court in *In re Fritch*, 23 U.S.P.Q. 2d 1780, 1783-1784 (Fed. Cir. 1992): "The mere fact that the prior art may be modified in the manner suggested by the Office Action does not make the modification obvious unless the prior art suggests the desirability of the modification." Also, the Examiner is respectfully reminded that for the Section 103 rejection to be proper, both the suggestion of the claimed invention and the expectation of success must be founded in the prior art, and not Applicants' disclosure. *In re Dow*, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988).

Applying the law to the instant facts, the references relied upon by the Office Action does not disclose, suggest or enable Applicants' invention. In particular, there was no expectation of success in Quelle, *et al.* Applicants maintain that Quelle *et al.* do **not** teach *in vivo* activity, despite the misinterpretation by the Examiner of previous statements made on record by the Applicants. Applicants submit that Quelle *et al.* lack experimental evidence demonstrating that the *in vitro* activity of their protein translates to *in vivo* erythropoietic activity. In fact, as submitted on page 2, section 3 of the Cox Declaration, Quelle *et al.* "have characterized the 'lack of in vivo activity' of insect-cell derived EPO as a function of the absence of sialic acid. Quelle at 656". Quelle *et al.* did not expect that the insect-cell derived EPO of the present invention would be active in the routine *in vivo* bioassays used to determine the specific activity of the EPO.

Moreover, as discussed in Saghatelian *et al.* and in the Cox Declaration, *in vitro* activity does not necessarily translate to *in vivo* activity. In particular, page 8, section 5 of the Cox Declaration states that the invention "is not obvious as one could not have predicted that the inventive EPO would have achieved the results that it does, e.g. increased reticulocyte counts, indicating in vivo activity and stimulation of erythropoiesis…".

In view of the foregoing and the arguments presented against the Section 102(b) rejection, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

REQUEST FOR INTERVIEW

If any issue remains as an impediment to further examination and/or allowance, an interview with the is respectfully requested, prior to issuance of any paper other than a Notice of Allowance; and, the Examiner is respectfully requested to contact the undersigned to arrange a mutually convenient time and manner for such an interview.

CONCLUSION

In view of the remarks, amendments and enclosures herewith and those of record, the application is in condition for allowance. Favorable reconsideration of the rejections of the application and prompt issuance of a Notice of Allowance, or an interview at a very early date with a view to placing the application in condition for allowance, are earnestly solicited. The undersigned looks forward to hearing favorably from the Examiner at an early date.

Respectfully submitted,

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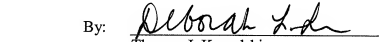
By: 

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